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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/719,571	09/25/96	ANDERSON D	A-63899-1

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FLEHR HOHBACH TEST ALBRITTON & HERBERT
FOUR EMBARCADERO CENTER
SUITE 3400
SAN FRANCISCO CA 94111-4187

EXAMINER	
GRUN, J	

ART UNIT	PAPER NUMBER
1641	9

DATE MAILED: 10/26/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/719,571	Applicant(s) ANDERSON
	Examiner James L. Grun, Ph.D.	Group Art Unit 1641

☒ Responsive to communication(s) filed on *3 Aug 1998*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 2, 4-8, and 12-15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 4-8, and 12-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The amendment filed 03 August 1998 is acknowledged and has been entered. Claim 15 is newly added. Claims 3 and 9-11 have been cancelled. Claims 1-2, 4-8, and 12-15 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The amendment filed 03 August 1998 is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: support for the additional columns and data added to Table 2, on page 24, and to Table 3, on page 30, are not found in the specification as originally filed. Applicant's argument that the tables, as amended, are as disclosed in Provisional Application 60/025,579 is not found persuasive. Unless expressly incorporated by reference in the original non-provisional disclosure, the disclosure of the Provisional Application does not form part of the original disclosure of the Non-provisional Application.

Applicant is required to cancel the new matter in the response to this Office action.

Applicant's indication that the requirement for submission of formal drawings is being held in abeyance pending the indication of allowable subject matter is acknowledged.

The specification is objected to and claims 4 and 12 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record that the specification, while being enabling for antibodies specific for RET antigen expressed in mice and rats, does not reasonably provide enablement for any other reagent which specifically binds RET antigen.

Applicant urges that binding reagents other than antibodies may be identified with isolated RET and used in the method. This is not found persuasive for the reasons of record that Applicant provides no description or guidance for any binding reagent other than antibodies for rat and mouse RET. It is unpredictable whether another specific binding reagent other than antibodies can be obtained and entirely unknown what compounds to even try in Applicant's argued screening assay to predictably obtain such a reagent. Random experimentation without any guidance from Applicant is undue experimentation. Applicant's argued screening method is merely an invitation for another, after undue experimentation, to find and use what Applicant claims as the invention and, thus, does not enable making and using any particular reagent other than antibodies.

The specification is objected to and claims 1-2 are rejected under 35 U.S.C. § 112, first paragraph, because these claims, as instantly amended, contain subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention or to use the invention commensurate in scope with these claims. Applicant discloses the binding of monoclonal antibodies to cell surface RET as a transient labelling step during cell separation or cell identification, and provides no description or guidance for how or why one uses the antibodies themselves for any other purpose after they have already been used for cell labelling. Absent further guidance from Applicant, one would know of no further use for a monoclonal antibody bound to a cell as instantly claimed other than in the specific assay in which it was used to label the particular cell to which it was bound.

Claims 1-2, 4-7, and 12-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-2, 4-7, and 12-15, the metes and bounds of what is or is not encompassed by a "RET antigen" remain entirely unclear. Applicant urges that the specification teaches that the sequence of RET is known and reported in the literature. This is not found persuasive because the claims are not limited to RET or a fragment thereof as the specification discloses that RET or a "part" thereof "may be used as a RET antigen". The metes and bounds of what else may be encompassed by recitation of a "RET antigen" cannot be determined from this inclusive definition.

Claims 1-2, 4-8, and 12-15 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Lo et al (Neuron 15: 527-539, 1995) for reasons of record.

Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive. That Applicant now "believes" Liching Lo to be an inventor does not overcome the rejection in the absence of compliance with the requirements of 37 C.F.R. § 1.48.

Claims 1-2, 4-8, and 12-15 are also rejected under 35 U.S.C. 102(f)/(g) because, in light of Applicant's belief that Liching Lo is a co-inventor of the claimed subject matter, the instant inventive entity did not invent the claimed subject matter.

Claim 8 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Stemple et al (Cell 71: 973-985, 1992) for reasons of record in the prior rejection of the similar subject matter of claims 8-11.

Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive. Notwithstanding Applicant's arguments to the contrary, Stemple et al disclose cloned cells (i.e. substantially pure) having the developmental potentials of the instant cell populations as disclosed. Indeed, Applicant admits that at least some of the cells cloned with the method of Stemple et al are "Nps" (see e.g. specification page 26).

Claims 1-2 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Martucciello et al. This is a NEW GROUND

of rejection necessitated by Applicant's amendments. In addition to the teachings of the reference set forth in the prior Office action, the reference teaches the binding of the anti-RET monoclonal antibodies to cells in intestinal plexuses. To the extent that the claims appear, as previously, directed to a monoclonal antibody, recitations of intended use, such as the antibodies being bound to a particular cell population have been accorded no weight, and the anti-RET monoclonal antibodies of the reference clearly anticipate the monoclonal antibodies as claimed for reasons of record. Alternatively, if it is Applicant's intention to claim a composition of cells having bound antibodies, the reference does not disclose the types of cells bound by the antibodies in the method of the reference, as admitted by Applicant, and thus, their relationship to the cell populations as claimed cannot be determined. The Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive as there is no factual evidence of a difference between what is disclosed in the reference and what is instantly claimed.

Claim 8 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Vescovi et al. This is a NEW GROUND of rejection necessitated by Applicant's amendments.

Claim 8 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Reynolds et al (Soc. Neurosci. Abstr. 18: 1107, Abstract 467.3, 1992). This is a NEW GROUND of rejection necessitated by Applicant's amendments.

Claim 8 is rejected under 35 U.S.C. § 102(e) as being clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Boss et al (US 5,411,883). This is a NEW GROUND of rejection necessitated by Applicant's amendments.

As set forth, the references teach substantially pure neural progenitor cell populations. The relationships of these populations to those as instantly claimed cannot be determined from the disclosures therein or from the instant disclosure. Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive as there is no factual evidence of a difference between the cell populations disclosed in the references and those as instantly claimed. Applicant's arguments with regard to the different methods of isolation are not dispositive of the issues as the process of making a product does not serve to distinguish the same product made by another method from itself.

Claims 1-2 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hesketh in view of Martucciello et al, Campbell, Harlow et al, and Maurer et al for reasons of record. The claims appear directed, as previously, to a monoclonal antibody. Recitations of intended use, such as the antibodies being bound to a particular cell population have been accorded no weight.

Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive.

In response to Applicant's arguments that there are no specific suggestions to combine the references, the Examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In this case, for the reasons of record, ample motivations to elicit antibodies to the RET protein are provided with, for reasons of record, an extremely reasonable expectation of success.

Claims 1-2, 4-8, and 12-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lo et al (Perspectives Dev. Neurobiol. 2: 191-201, 1994), Stemple et al (Dev. Biol. 159: 12-23, 1993), Stemple et al (Cell 71: 973-985, 1992), and Martucciello et al for reasons of record in the prior rejection of the similar subject matter of claims 4-14.

Applicant's arguments filed 03 August 1998 have been fully considered but they are not deemed to be persuasive.

Again, in response to Applicant's arguments that there are no specific suggestions to combine the references, the Examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969). Notwithstanding Applicant's arguments to the contrary, in this case, for the reasons of record, ample motivations to isolate RET+ cells are provided with, for reasons of record, an extremely reasonable

expectation of success using the conventional methods of the references. Indeed, Lo et al provide the specific suggestion that cells expressing this marker should be isolated for further testing.

In response to Applicant's arguments that RET expression helps identify the lineage of neural crest stem cells, the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The Examiner would note that Applicant does not describe and is not claiming a method for identifying the lineage of neural crest stem cells, only a method of neural progenitor cell enrichment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (703) 308-3980. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James C. Housel, SPE, can be reached on (703) 308-4027. The fax phone numbers for official communications to Group 1640 are (703) 305-3014 or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JLG

James L. Grun, Ph.D.
October 16, 1998

James C. Housel
JAMES C. HOUSEL 10/16/98
SUPERVISORY PATENT EXAMINER